REMARKS

This Response, filed in reply to the Office Action dated June 6, 2008, is believed to be fully responsive to each point of objection and rejection raised therein. Accordingly, favorable reconsideration on the merits is respectfully requested.

Claims 1-10 are rejected. Claims 11-20 are withdrawn from consideration as being directed to non-elected inventions. Although page 2 of the Office Action indicates that Claims 1-10 are withdrawn, such appears to be a typographical error because Claims 1-10 were elected by Applicants, and are rejected in the outstanding Office Action. Consideration of the remarks herein is respectfully requested.

Claim to Priority

Applicants thank the Examiner for acknowledging Applicants' claim to foreign priority, and receipt of all the priority documents from the International Bureau.

Withdrawn Rejections

1. Applicants thank the Examiner for withdrawal of the rejection of Claims 1-4 under 35 U.S.C § 112, as set forth in the previous Office Action. On page 2 of the Office Action, the Examiner notes that recitation of "said microbe produces iturin A" makes clear that the instant method "is not an [iturin A] sequestering or collection method[,] or [a method in which] additional iturin A was not added to the medium."

2. Applicants thank the Examiner for withdrawal of the rejection of Claims 1-10 under 35 U.S.C § 103(a) over Phae *et al.* and Tanaka *et al.* On page 2 of the Office Action, the

Examiner states that Applicants' amendment makes clear that "the [iturin A] in this method is produced by the microbe and not added externally."

Regarding the Examiner's reasons for withdrawal of the rejection of Claims 1-10 under 35 U.S.C § 103(a), namely that Applicants made clear that iturin A is produced by the microbe, Applicants note that the Examiner previously relied upon Phae *et al.* to "teach a *Bacillus subtilis* that produces and accumulates iturin A and its homologues in a liquid medium ..." (Emphasis added.) Page 4 of the Office Action mailed October 12, 2007. Applicants traversed the rejection under 35 U.S.C § 103(a) through argument alone, and the traversal arguments therein did not require, nor were they directed to, the claims as amended. Further, the new grounds of rejection set forth in the outstanding Office Action were not necessitated by Applicants' amendment because Phae *et al.* was already relied upon by the Examiner as disclosing a *Bacillus subtilis* that produces iturin A and its homologues in a liquid medium. For this reason, Applicants submit that the outstanding Office Action is prematurely final, and therefore request that the finality of the outstanding Office Action be withdrawn.

Claims 1, 2, 5, 8 and 9 are Patentable Under 35 U.S.C. § 102(b)

On page 3 of the Office Action, the Examiner rejects Claims 1, 2, 8 and 9 under 35 U.S.C. 102(b) as being anticipated by Ohno *et al.* (*Process Biochemistry*, 1996, Vol. 31, 8:801-806) (hereinafter "Ohno #1"). From the Examiner's comments on page 3 of the Office Action, the Examiner appears to indicate that Claims 1, 2, 5, 8 and 9 are included in the rejection. Accordingly, Applicants have addressed the rejection as it applies to Claims 1, 2, 5, 8 and 9.

In making the rejection, the Examiner asserts that Ohno #1 disclose a method for cultivating iturin A in a liquid medium comprising 15 g of a solid substrate of soaked soybean

powder extract (i.e., soaked okara), 0.8 mL of glucose, 0.075 mL of KH_2PO_4, and 3 mL of *Bacillus subtilis* NB22 in 3S medium. The Examiner contends that the total volume of liquid media added to the okara fermentation is 4.1 ml. The Examiner further contends that this liquid culture was fermented to produce 1.65 g of iturin A per kilogram of wet okara, and since 15 g of okara was used in the above-described fermentation, 24.75 g of iturin A was produced. The Examiner concludes that because the volume of the liquid medium was 4.1 ml, such a method provides an iturin A concentration of 6 g/mL, or 6000 g/L iturin A.

Applicants respectfully disagree, and traverse the rejection, respectfully, on the following grounds.

First, Applicants refer the Examiner to the Abstract of Ohno #1, which states that "[t]he possibility of the utilization of soybean curd residue, okara, for the production of a lipopeptide antibiotic, iturin A, in **solid state** fermentation (SSF)... was investigated." (Emphasis added.) That is, the method of Ohno #1 is directed entirely to solid-state fermentation of okara to produce iturin A, using a solid medium, and is, by definition, not fermentation in a "liquid medium." Thus, Ohno #1 do not anticipate the claimed invention at least because Ohno #1 do not disclose, either expressly or inherently, "cultivating a *Bacillus* microbe having an ability to produce iturin A and its homologues in a liquid medium ...," as recited in Claim 1. A claim is anticipated *only* if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.

Second, Applicants point out "okara" is not a soybean extract, but rather, is residue which remains following soybean extraction, as discussed in page 802, 1st column, of Ohno #1.

Third, even assuming *arguendo* that the fermentation medium of Ohno #1 were to be considered a liquid medium, which it clearly is not, the 15 g of okara would therefore *necessarily*

have to be included in the "volume" since the instant claims recite a "liquid medium **containing** 2% mass or more of soybean powder or its extract." In arriving at a value of 6g/mL (which Applicants point out should be 6g/L, according to the Examiner's own rationale), the Examiner has clearly failed to consider the *necessary* increase in volume upon addition of the okara. Nevertheless, Applicants again point out that the method of Ohno #1 is directed solely to **solid state** fermentation, and thus such a comparison is inapt from the outset.

Further still, Applicants point out that Ohno #1 expressly disclose that their method is not performed using a liquid culture, by stating that "[t]he concentration of total iturin A produced is 6-8 times higher than that in liquid fermentation ..." (Emphasis added.) Thus, it is clear that Ohno #1 do not disclose iturin A production in a liquid medium, as recited in the instant claims.

Accordingly, Ohno #1 fail to teach each and every element of the claims, either expressly or inherently, as is required to maintain a finding of anticipation.

Withdrawal of the rejection is respectfully requested.

Claims 1-3 and 5-9 are Patentable Under 35 U.S.C. § 103

On page 4 of the Office Action, the Examiner rejects Claims 1-3 and 5-9 under 35 U.S.C. 103(a) as obvious over Ohno #1 as applied to Claims 1, 2, 5, 8 and 9 above, in view of Ohno *et al.* (*J. of Fermentation And Bioengineering*, 1995, Vol. 80, 5:517-519) (hereinafter "Ohno #2) and Ohno *et al.* (*Biotechnology Letters*, 1992, Vol. 14, 9:817-822) (hereinafter "Ohno #3").

The Examiner states that Claims 1, 2, 5, 8 and 9 are rejected for the reasons set forth above, and therefore the rejection of these claims is duplicative.

Regarding Claim 3, the Examiner asserts that Ohno #1 do not disclose how much, if any, surfactin is produced by *B. subtilis* NB22. However, the Examiner takes the position that given

the similarity between the instant strains, and those of the cited references, the recited characteristic is presumed to be inherent in the prior art strains. The Examiner also contends that it would have been obvious to the skilled artisan that the strains of the prior art do not produce surfactin, because iturin A and surfactin are both cyclic polypeptides consisting of 7 amino acids, and it would be recognized that the centrifugation, filtration and methanol extraction steps employed by Ohno #1 would not discriminate between these peptides such that both polypeptides would be detected by HPLC. However, the Examiner alleges that Ohno #1 do not detect surfactin. The Examiner also cites to Ohno #2 for support, who allegedly disclose *B. subtilis* RB14, which produces iturin A and surfactin simultaneously, and that such a strain contrasts with *B. subtilis* NB22, which is stated to only produce iturin A, citing page 517, column 1, paragraph 1.

Regarding Claims 6 and 7, the Examiner asserts that Ohno #1 only disclose the use of *Bacillus subtilis* NB22 to ferment and obtain iturin A, or its homologues, from a soybean extract, and Ohno #1 does not disclose use of *Bacillus subtilis* SD142, or a mutant thereof. The Examiner takes the position that as the strains of the prior art have the same species and genus classification as the instant strain, and share the property of being able to produce iturin A, and its homologues, the strains are essentially the same, absent evidence to the contrary.

Applicants respectfully disagree with the rejection, and traverse, respectfully, on the following grounds.

Initially, as Claims 1, 2, 5, 8 and 9 are rejected for the same reasons as set forth in the rejection under section 102, discussed above, the rejection of these claims is inapt for the reasons provided above.

Regarding Claims 3, 6 and 7, Applicants point out that the addition of Ohno #2 and Ohno #3 do not cure the deficiencies of Ohno #1, and as mentioned above, Ohno #1 is a defective reference. Specifically, none of the cited references disclose the production of iturin A, or its homologues to a concentration of 1.5 g/L or more, in a liquid medium. Ohno #2 and Ohno #3 are also directed solely to the production of iturin A by solid-state fermentation, thus the addition of Ohno #2 and Ohno #3 does nothing to cure the deficiencies of the primary reference. Accordingly, neither Ohno #1 alone, nor Ohno #1 in combination with Ohno #2 and Ohno #3 teach, suggest or otherwise render obvious each and every element of the claims, as is required to maintain a rejection under 35 U.S.C. § 103.

Additionally, regarding the Examiner's contention that it would have been obvious to the skilled artisan that the strains of the prior art do not produce surfactin, because iturin A and surfactin are both cyclic polypeptides consisting of 7 amino acids, and as such it would be recognized that the centrifugation, filtration and methanol extraction steps employed by Ohno #1 would not discriminate between these peptides such that both polypeptides would be detected by HPLC, Applicants respectfully point out that the art-recognized conditions for detecting iturin A and surfactin are distinct, and such is why Ohno #1 is unable to detect surfactin.

Withdrawal of the rejection is respectfully requested.

Claims 1-10 are Patentable Under 35 U.S.C. § 103, for Obviousness

On page 7 of the Office Action, the Examiner rejects Claims 1-10 under 35 U.S.C. 103(a) as being unpatentable over Ohno #1, as applied to Claims 1, 2, 5, 8 and 9 above, in view of Ohno #2 and Ohno #3. The Examiner states that Claims 1-3 and 5-9 are rejected for the reasons set forth above (i.e., for those reasons as set forth on pages 3-6 of the Office Action). Thus, the

rejection is again duplicative inasmuch as Claims 1-3 and 5-9 are not rejected on any new grounds.

Regarding Claim 4, the Examiner asserts that the subject matter of this claim would be obvious to one of skill in the art as they would recognize that KH_2PO_4 and K_2HPO_4 are both phosphates, and that substituting one for the other would have little effect on the medium. The Examiner concludes that both are art-recognized equivalents, used for the same purpose in culture media, and therefore it would be obvious to make such a substitution in the absence of evidence of criticality of one over the other.

Regarding Claim 10, the Examiner asserts that although Ohno #1 teach that iturin A is isolated with methanol, Ohno #1 do not disclose drying of iturin A. However, the Examiner asserts that one of ordinary skill in the art would readily apply the steps of roto-evaporation or vacuum-drying to the method of Ohno #1 to obtain a dry product that is easier to store and handle for future experiments.

Applicants respectfully disagree with the rejection, and traverse the rejection on the following grounds.

Initially, as Claims 1-3 and 5-9 are rejected for the same reasons as set forth in the rejections set forth above, the rejection of these claims is inapt for the reasons provided above.

Regarding Claims 4 and 10, Applicants point out that the addition of Ohno #2 and Ohno #3 do not cure the deficiencies of Ohno #1, and as mentioned above, Ohno #1 is a defective reference. Specifically, none of the cited references disclose the production of iturin A, or its homologues to a concentration of 1.5 g/L or more, in a liquid medium. Ohno #2 and Ohno #3 are also directed solely to the production of iturin A by solid-state fermentation, thus the addition of Ohno #2 and Ohno #3 does nothing to cure the deficiencies of the primary reference.

Accordingly, neither Ohno #1 alone, nor Ohno #1 in combination with Ohno #2 and Ohno #3 teach, suggest or otherwise render obvious each and every element of the claims, as is required to maintain a rejection under 35 U.S.C. § 103.

Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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